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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,579	01/25/2001	Hector F. DeLuca	960296.95700	4517

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,579	DELUCA ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/19/2002, 11/18/2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examinati n Und r 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Nov 18, 2002, Aug 19, 2002 has been entered.

Claims 1-5 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing not eliminating the risk of the onset of Type I diabetes in patients with autoantibodies towards glutamic acid decarboxylase or insulin, does not reasonably provide enablement for methods of eliminating the onset of all forms of diabetes in any human patients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In particular, the specifications fails to enable the skilled artisan to practice the invention without undue experimentation.

In re Wands provides several factors in determining whether the specification of an application allows the skilled artisan to practice the invention without undue

experimentation. See 858 F.2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988). Having said factors in mind, the instant specification fails to reasonably provide enablement for methods of eliminating the claimed condition.

First, the state of the prior art concerning methods of eliminating the onset of diabetes in a human patient is unpredictable. There are no guidelines currently setting forth how to eliminate the onset of diabetes in general. Accordingly, there is no predictability in the art concerning eliminating the onset or reducing the risk thereof among susceptible patients.

Further the specification of instant application does not describe the correlation between the instant *in vivo* example and the induced diabetes model in NOD mice samples and the whole population of patients that can suffer from various types of diabetes i.e. type II diabetes, diabetes secondary to pancretactomy or pancreas transplant etc... The Example in the specification is only a model for type I diabetes and that is all. Thus, the amount of guidance presented in the specification fails to present a required amount of guidance to perform the claimed method within the whole population of diabetic patients without undue experimentation.

Moreover, the specification does not provide direct evidence associating the absolute elimination of diabetes in patients who a used vitamin D compound. At best, the example solely showed an improved risk/benefit reduction among the sample population. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the entire scope of the presently claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 is rejected because the scope of the claim is not clear. Applicant is encouraged to use proper Markush language. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. When materials recited in a claim are so related as to constitute a proper Markush group, they may be recited in the conventional manner, or alternatively. For example, if "wherein R is a material selected from the group consisting of A, B, C and D" is a proper limitation, then "wherein R is A, B, C or D" shall also be considered proper. See MPEP 2173.

In the instant case, claim 3, at page 16, line 6-page 17, line 3 recite limitations such as: "where B1 and B2 can be selected," "can have a ß or α configuration, "R may represent the following side chain...may have an S or R configuration," "R^8 may be H or CH_3," and "may be replaced by an O, S, or N atom." The use of such language is confusing as to appropriately ascertaining the scope of the claim and whether such limitations are a part of claim or not. Examiner suggests using appropriate Markush language or changing "can be or may be" to "is or selected from the group."

Claim Rejecti ns - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by DeWille et al.

The instant claims are directed to methods of eliminating onset of diabetes comprising orally administering to a patient an effective amount of 1α – hydroxy vitamin D.

DeWillis discloses methods of orally administering vitamin D_3 containing beverages to consumers (abstract, examples 12-16). Vitamin D_3 is a 1α – hydroxy vitamin D. In process claims, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since DeWillis meets all the process steps of the instant claims it inherently meets the intended use of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathieu et al (Diabetologia, 1994; 37: 552-558) in view of EURODIAB (PTO-892, filed 10/10/01), Mauricio et al (PTO-892, filed 10/10/01) DeWille et al (US 5,817,351; PTO-892, filed 10/10/01) and Facts and Comparison 1999 (pages 11-15).

Mathieu explicitly teaches that using 1, 25 dihydroxy vitamin D_3 prevents autoimmune diabetes in NOD mice (see abstract, entire pages 555-557). Mathieu does not employ oral vit D compound.

EURODIAB and Muricio collectively provides the understanding in the art that vitamin D and analogues thereof, including 1, α-hydroxyvitamin D_3, improves the symptoms of autoimmune diseases and diabetes (see EURODIAB, abstract; Mathieu, pp 552-556; Muricio et al pp 64, 1st col, 2nd paragraph). EURODIAB for example teaches methods of delaying the onset of diabetes in a human patient using vit D compounds (see p. 51, summary, col 1, line 15-col 2, line 2, entire p 52-54). Mauricio teaches 1, 25 vit D_3 and its possible role in preventing Insulin Dependent Diabetes Mellitus (IDDM) (p 63-64).

DeWille is used to show that all vitamin D such as 1 α vitamin D can be prepared and used orally. (see abstract, examples 12-16). Facts merely is used to show various forms of oral vitamin D formulations, liquid, capsules, tabets, that are conventionally prepared in the art (pages 11-15, see specifically Cholecalciferol® and Rocaltrol ®or Calderol®).

Therefore, eventhough Matieu did not specifically teach the use of oral Vitamin D supplementation in treating diabetes, it would have been obvious to one of ordinary skill in the art at the time of invention to employ any oral form of vitamin D3, as taught by DeWillie and Facts, because as taught by Matieu, EURODOB and Mauricio, the ordinary artisan would have had a reasonable expectation of success in reducing the risk of autoimmune diabetes in susceptible patients. Further, absence of showing unexpected results, route of administration is a matter of design choice and preparing oral formulations of vit D_3, as shown by DeWille and Facts, are well within purview of the ordinary artisan.

C nclusi n

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

ss
February 8, 2003

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200